



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> :  A61K 31/365		A3	(11) International Publication Number: WO 98/01100  (43) International Publication Date: 15 January 1998 (15.01.98)
(21) International Application Number: PCT/US97/11792 (22) International Filing Date: 3 July 1997 (03.07.97) (30) Priority Data: 60/021,420      9 July 1996 (09.07.96)      US 9617898.3      28 August 1996 (28.08.96)      GB 60/029,351      31 October 1996 (31.10.96)      US (71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): MITCHEL, Yale, B. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). TOBERT, Jonathan, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).		(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.          Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 12 February 1998 (12.02.98)	
(54) Title: METHOD FOR TREATING HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (57) Abstract <p>Homozygous familial hypercholesterolemia can be treated in patients suffering with this condition by administering a therapeutically effective amount of simvastatin. Dosages above 40 mg/day, and more particularly at or above 80 mg/day, were found to effectively reduce the LDL cholesterol levels in these patients.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China			PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/11792

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/365

US CL :514/460

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/460

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CHEMICAL ABSTRACTS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. November 1994, Vol. 19:344, pages 1383-9 (1994) (Abstract).	1-9
A	US, 5,393,893 A (KUBELA et al.) 28 February 1995, see entire document.	1-9
A	US, 4,997,849 A (PETUCH et al.) 05 March 1991, see entire document.	1-9

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*A*	document defining the general state of the art which is not considered to be of particular relevance	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*E*	earlier document published on or after the international filing date	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*L*	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*O*	document referring to an oral disclosure, use, exhibition or other means	*A*	document member of the same patent family
*P*	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

03 NOVEMBER 1997

Date of mailing of the international search report

15 DEC 1997

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JAMES H. REAMER

Telephone No. (703) 308-1235

185/39/61  
DIALOG(R)File 345:Inpadoc/Fam.& Legal Stat  
(c) 2001 EPO. All rts. reserv.

13245748

Basic Patent (No,Kind,Date): GB 9617898 A0 19961009 <No. of Patents: 007>

Patent Family:

Patent No	Kind	Date	Applic No	Kind	Date	
AU 9736672	A1	19980202	AU 9736672	A	19970703	
AU 9742289	A1	19980202	AU 9742289	A	19970703	
AU 9743261	A1	19980202	AU 9743261	A	19970703	
GB 9617898	A0	19961009	GB 9617898	A	19960828	(BASIC)
WO 9801116	A1	19980115	WO 97US12426	A	19970703	
WO 9801100	A2	19980115	WO 97US11792	A	19970703	
WO 9801119	A2	19980115	WO 97US10867	A	19970703	

Priority Data (No,Kind,Date):

GB 9617898 A 19960828  
US 21420 P 19960709  
US 29351 P 19961031  
WO 97US12426 W 19970703  
WO 97US11792 W 19970703

BEST AVAILABLE COPY

WO 97US10867 W 19970703

PATENT FAMILY:

AUSTRALIA (AU)

Patent (No,Kind,Date): AU 9736672 A1 19980202  
THERAPY FOR COMBINED HYPERLIPIDEMIA (English)  
Patent Assignee: MERCK & CO INC  
Author (Inventor): MITCHEL YALE B; MELINO MICHAEL R  
Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031; WO 97US12426 W 19970703  
Applic (No,Kind,Date): AU 9736672 A 19970703  
IPC: \* A61K-009/20  
CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S  
Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191  
Language of Document: English  
Patent (No,Kind,Date): AU 9742289 A1 19980202  
METHOD FOR TREATING HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (English)  
Patent Assignee: MERCK & CO INC  
Author (Inventor): MITCHEL YALE B; TOBERT JONATHAN A  
Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031; WO 97US11792 W 19970703  
Applic (No,Kind,Date): AU 9742289 A 19970703  
IPC: \* A61K-031/00  
CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S  
Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191  
Language of Document: English  
Patent (No,Kind,Date): AU 9743261 A1 19980202  
PHARMACEUTICAL COMPOSITIONS (English)  
Patent Assignee: MERCK & CO INC  
Author (Inventor): MITCHEL YALE B; TOBERT JONATHAN A  
Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031; WO 97US10867 W 19970703  
Applic (No,Kind,Date): AU 9743261 A 19970703  
IPC: \* A61K-031/00  
CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S  
Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191  
Language of Document: English

GREAT BRITAIN (GB)

Patent (No,Kind,Date): GB 9617898 A0 19961009  
METHOD FOR TREATING HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (English)  
Patent Assignee: MERCK & CO INC  
Priority (No,Kind,Date): GB 9617898 A 19960828  
Applic (No,Kind,Date): GB 9617898 A 19960828  
Language of Document: English

WORLD INTELLECTUAL PROPERTY ORGANIZATION, PCT (WO)

Patent (No,Kind,Date): WO 9801116 A1 19980115  
THERAPY FOR COMBINED HYPERLIPIDEMIA (English)  
Patent Assignee: MERCK & CO INC (US); MITCHEL YALE B (US); MELINO  
MICHAEL R (US)  
Author (Inventor): MITCHEL YALE B (US); MELINO MICHAEL R (US)  
Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031  
Applic (No,Kind,Date): WO 97US12426 A 19970703  
Designated States: (National) AL; AM; AU; AZ; BB; BG; BR; BY; CA; CN;  
CZ; EE; GE; HU; IL; IS; JP; KG; KR; KZ; LK; LR; LT; LV; MD; MG; MK;

MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; SL; TJ; TM; TR; TT; UA; US;  
UZ; VN; YU; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM (Regional) GH; KE;  
LS; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE;  
IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE;  
SN; TD; TG

Filing Details: WO 100000 With international search report

IPC: \* A61K-009/20

CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S;  
128(09)097716K

Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191; C  
98-110207

Language of Document: English

Patent (No,Kind,Date): WO 9801100 A2 19980115

METHOD FOR TREATING HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (English)

Patent Assignee: MERCK & CO INC (US); MITCHEL YALE B (US); TOBERT  
JONATHAN A (US)

Author (Inventor): MITCHEL YALE B (US); TOBERT JONATHAN A (US)

Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031

Applic (No,Kind,Date): WO 97US11792 A 19970703

Designated States: (National) AL; AM; AU; AZ; BA; BB; BG; BR; BY; CA;  
CN; CU; CZ; EE; GE; HU; IL; IS; JP; KG; KR; KZ; LC; LK; LR; LT; LV;  
MD; MG; MK; MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; SL; TJ; TM; TR;  
TT; UA; US; UZ; VN; YU; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM  
(Regional) GH; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI  
; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA;  
GN; ML; MR; NE; SN; TD; TG

Filing Details: WO 130000 With international search report; Before  
expiration of time limit for amending the claims and to be  
republished in the event of the receipt of the amendments

IPC: \* A61K

CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S;  
128(09)097715J

Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191; C  
98-110203

Language of Document: English

Patent (No,Kind,Date): WO 9801119 A2 19980115

PHARMACEUTICAL COMPOSITIONS (English)

Patent Assignee: MERCK & CO INC (US); MITCHEL YALE B (US); TOBERT  
JONATHAN A (US)

Author (Inventor): MITCHEL YALE B (US); TOBERT JONATHAN A (US)

Priority (No,Kind,Date): GB 9617898 A 19960828; US 21420 P  
19960709; US 29351 P 19961031

Applic (No,Kind,Date): WO 97US10867 A 19970703

Designated States: (National) AL; AM; AU; AZ; BB; BG; BR; BY; CA; CN;  
CZ; EE; GE; HU; IL; IS; JP; KG; KR; KZ; LK; LR; LT; LV; MD; MG; MK;  
MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; SL; TJ; TM; TR; TT; UA; US;  
UZ; VN; YU; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM (Regional) GH; KE;  
LS; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE;  
IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE;  
SN; TD; TG

Filing Details: WO 300000 Without international search report and to  
be republished upon receipt of that report

IPC: \* A61K-031/00

CA Abstract No: \* 128(09)097715J; 128(09)097716K; 128(11)132435S;  
128(11)132435S

Derwent WPI Acc No: \* C 98-110203; C 98-110207; C 98-145191; C

98-145191  
Language of Document: English

WORLD INTELLECTUAL PROPERTY ORGANIZATION, PCT (WO)

Legal Status (No, Type, Date, Code, Text):

WO 9801100	P	19960709	WO AA	PRIORITY CLAIMED
		US 21420	P	19960709
WO 9801100	P	19960828	WO AA	PRIORITY (PATENT)
		GB 9617898	A	19960828
WO 9801100	P	19961031	WO AA	PRIORITY CLAIMED
		US 29351	P	19961031
WO 9801100	P	19970703	WO AE	APPLICATION DATA (APPL. DATA)
		WO 97US11792	A	19970703
WO 9801100	P	19980115	WO AK	DESIGNATED STATES CITED IN A PUBLISHED APPLICATION WITHOUT SEARCH REPORT (DESIGNATED STATES CITED IN A PUBLISHED APPL. WITHOUT SEARCH REPORT)
		AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AM AZ BY KG KZ MD RU TJ TM		
WO 9801100	P	19980115	WO AL	DESIGNATED COUNTRIES FOR REGIONAL PATENTS CITED IN A PUBLISHED APPLICATION WITHOUT SEARCH REPORT (DESIGNATED COUNTRIES FOR REGIONAL PATENTS CITED IN A PUBLISHED APPL. WITHOUT SEARCH REPORT)
		GH KE LS MW SD SZ UG ZW AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG		
WO 9801100	P	19980115	WO A2	PUBLICATION OF THE INTERNATIONAL APPLICATION WITHOUT THE INTERNATIONAL SEARCH REPORT (PUB. OF THE INTERNATIONAL APPL. WITHOUT THE INTERNATIONAL SEARCH REPORT)
WO 9801100	P	19980326	WO DFPE	REQUEST FOR PRELIMINARY EXAMINATION FILED PRIOR TO EXPIRATION OF 19TH MONTH FROM PRIORITY DATE
WO 9801100	P	19980520	WO 121	EP: PCT APP. ART. 158 (1) (EP: PCT ANM. ART. 158 (1))
WO 9801100	P	19990604	WO NENP	<u>NON-ENTRY INTO THE NATIONAL PHASE IN:</u>
		<u>JP</u>	1998505308	
WO 9801100	P	20000109	WO NENP	<u>NON-ENTRY INTO THE NATIONAL PHASE IN:</u>
		<u>CA</u>		
WO 9801100	P	20000209	WO 122	EP: PCT APP. NOT ENT. EUROP. PHASE (EP: PCT ANM. NICHT IN EUROP. PHASE <u>ENG.</u> )
WO 9801116	P	19960709	WO AA	PRIORITY CLAIMED
		US 21420	P	19960709
WO 9801116	P	19960828	WO AA	PRIORITY (PATENT)
		GB 9617898	A	19960828
WO 9801116	P	19961031	WO AA	PRIORITY CLAIMED
		US 29351	P	19961031
WO 9801116	P	19970703	WO AE	APPLICATION DATA (APPL. DATA)

			DATA)
		WO 97US12426 A	19970703
WO 9801116	P	19980115 WO AK	DESIGNATED STATES CITED IN A PUBLISHED APPLICATION WITH SEARCH REPORT (DESIGNATED STATES CITED IN A PUBLISHED APPL. WITH SEARCH REPORT) AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KG KR KZ LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AM AZ BY KG KZ MD RU TJ TM
WO 9801116	P	19980115 WO AL	DESIGNATED COUNTRIES FOR REGIONAL PATENTS CITED IN A PUBLISHED APPLICATION WITH SEARCH REPORT (DESIGNATED COUNTRIES FOR REGIONAL PATENTS CITED IN A PUBLISHED APPL. WITH SEARCH REPORT) GH KE LS MW SD SZ UG ZW AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
WO 9801116	P	19980115 WO A1	PUBLICATION OF THE INTERNATIONAL APPLICATION WITH THE INTERNATIONAL SEARCH REPORT (PUB. OF THE INTERNATIONAL APPL. WITH THE INTERNATIONAL SEARCH REPORT)
WO 9801116	P	19980212 WO DFPE	REQUEST FOR PRELIMINARY EXAMINATION FILED PRIOR TO EXPIRATION OF 19TH MONTH FROM PRIORITY DATE
WO 9801116	P	19980506 WO 121	EP: PCT APP. ART. 158 (1) (EP: PCT ANM. ART. 158 (1))
WO 9801116	P	19990604 WO NENP	NON-ENTRY INTO THE NATIONAL PHASE IN: <u>JP 1998505391</u>
WO 9801116	P	20000109 WO NENP	<u>NON-ENTRY INTO THE NATIONAL PHASE IN:</u> <u>CA</u>
WO 9801116	P	20000112 WO 122	<u>EP: PCT APP. NOT ENT. EUROP. PHASE (EP: PCT ANM. NICHT IN EUROP. PHASE EING.)</u>
WO 9801119	P	19960709 WO AA	PRIORITY CLAIMED US 21420 P 19960709
WO 9801119	P	19960828 WO AA	PRIORITY (PATENT) GB 9617898 A 19960828
WO 9801119	P	19961031 WO AA	PRIORITY CLAIMED US 29351 P 19961031
WO 9801119	P	19970703 WO AE	APPLICATION DATA (APPL. DATA) WO 97US10867 A 19970703
WO 9801119	P	19980115 WO AK	DESIGNATED STATES CITED IN A PUBLISHED APPLICATION WITHOUT SEARCH REPORT (DESIGNATED STATES CITED IN A PUBLISHED APPL. WITHOUT SEARCH REPORT) AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KG KR KZ LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AM AZ BY KG KZ MD RU TJ TM
WO 9801119	P	19980115 WO AL	DESIGNATED COUNTRIES FOR REGIONAL PATENTS CITED IN A PUBLISHED APPLICATION WITHOUT SEARCH REPORT



(DESIGNATED COUNTRIES FOR REGIONAL PATENTS  
CITED IN A PUBLISHED APPL. WITHOUT SEARCH  
REPORT)

GH KE LS MW SD SZ UG ZW AT BE CH DE DK ES FI  
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI  
CM GA GN ML MR NE SN TD TG

WO 9801119	P	19980115	WO A2	PUBLICATION OF THE INTERNATIONAL APPLICATION WITHOUT THE INTERNATIONAL SEARCH REPORT (PUB. OF THE INTERNATIONAL APPL. WITHOUT THE INTERNATIONAL SEARCH REPORT)
WO 9801119	P	19980312	WO DFPE	REQUEST FOR PRELIMINARY EXAMINATION FILED PRIOR TO EXPIRATION OF 19TH MONTH FROM PRIORITY DATE
WO 9801119	P	19980506	WO 121	EP: PCT APP. ART. 158 (1) (EP: PCT ANM. ART. 158 (1))
WO 9801119	P	19990604	WO NENP	<u>NON-ENTRY</u> INTO THE NATIONAL PHASE IN: JP 1998505217
WO 9801119	P	19991110	WO 122	<del>EP: PCT APP. NOT ENT. EUROP.</del> PHASE (EP: PCT ANM. NICHT IN EUROP. PHASE EING.)
WO 9801119	P	20000109	WO NENP	<u>NON-ENTRY</u> INTO THE NATIONAL PHASE IN: <u>CA</u>

BEST AVAILABLE COPY